

What is claimed is:

1. An isolated, enriched, or purified nucleic acid molecule comprising a nucleic acid molecule selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6.

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2. An isolated, enriched, or purified nucleic acid molecule comprising a nucleic acid molecule which encodes a human OAT polypeptide selected from the group consisting of SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, and SEQ ID NO:12.

10 3. An isolated, enriched, or purified nucleic acid molecule which is complementary to any of the nucleic acid molecules of claims 1 and 2.

4. The isolated, enriched, or purified nucleic acid molecule of claim 1, wherein said nucleic acid molecule is SEQ ID NO:2.

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5. The isolated, enriched, or purified nucleic acid molecule of claim 1, wherein said nucleic acid molecule is SEQ ID NO:3.

20 6. The isolated, enriched, or purified nucleic acid molecule of claim 1, wherein said nucleic acid molecule is SEQ ID NO:4.

7. The isolated, enriched, or purified nucleic acid molecule of claim 1, wherein said nucleic acid molecule is SEQ ID NO:5.

25 8. The isolated, enriched, or purified nucleic acid molecule of claim 1, wherein said nucleic acid molecule is SEQ ID NO:6.

9. The isolated, enriched, or purified nucleic acid molecule of claim 2, wherein said nucleic acid molecule encodes a polypeptide that is SEQ ID NO:8.

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10. The isolated, enriched, or purified nucleic acid molecule of claim 2, wherein said nucleic acid molecule encodes a polypeptide that is SEQ ID NO:9.

11. The isolated, enriched, or purified nucleic acid molecule of claim 2, wherein said nucleic acid molecule encodes a polypeptide that is SEQ ID NO:10.

12. The isolated, enriched, or purified nucleic acid molecule of claim 2, wherein said
5 nucleic acid molecule encodes a polypeptide that is SEQ ID NO:11.

13. The isolated, enriched, or purified nucleic acid molecule of claim 2, wherein said nucleic acid molecule encodes a polypeptide that is SEQ ID NO:12.

10 14. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

15 (a) a nucleotide sequence which encodes a naturally occurring variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:8, wherein the nucleotide sequence hybridizes to a nucleic acid molecule comprising SEQ ID NO:2 under stringent conditions;

(b) a nucleotide sequence which encodes a naturally occurring variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:9, wherein the nucleotide sequence hybridizes to a nucleic acid molecule comprising SEQ ID NO:3 under stringent conditions;

20 (c) a nucleotide sequence which encodes a naturally occurring variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:10, wherein the nucleotide sequence hybridizes to a nucleic acid molecule comprising SEQ ID NO:4 under stringent conditions;

25 (d) a nucleotide sequence which encodes a naturally occurring variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:11, wherein the nucleotide sequence hybridizes to a nucleic acid molecule comprising SEQ ID NO:5 under stringent conditions; and

30 (e) a nucleotide sequence which encodes a naturally occurring variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:12, wherein the nucleotide sequence hybridizes to a nucleic acid molecule comprising SEQ ID NO:6 under stringent conditions.

15. An isolated nucleic acid molecule comprising a nucleotide sequence that has at least 83% identity to nucleotide sequence contained in SEQ ID NO:2, wherein the percent identity is calculated using the GAP-Alignment program in the GCG software package, using a gap weight of 5.0 and a length weight of 0.3.

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16. An isolated nucleic acid molecule comprising a nucleotide sequence that has at least 83% identity to nucleotide sequence contained in SEQ ID NO:3, wherein the percent identity is calculated using the GAP-Alignment program in the GCG software package, using a gap weight of 5.0 and a length weight of 0.3.

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17. An isolated nucleic acid molecule comprising a nucleotide sequence that has at least 61% identity to nucleotide sequence contained in SEQ ID NO:4, wherein the percent identity is calculated using the GAP-Alignment program in the GCG software package, using a gap weight of 5.0 and a length weight of 0.3.

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18. An isolated nucleic acid molecule comprising a nucleotide sequence that has at least 60% identity to nucleotide sequence contained in SEQ ID NO:5, wherein the percent identity is calculated using the GAP-Alignment program in the GCG software package, using a gap weight of 5.0 and a length weight of 0.3.

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19. An isolated nucleic acid molecule comprising a nucleotide sequence that has at least 60% identity to nucleotide sequence contained in SEQ ID NO:6, wherein the percent identity is calculated using the GAP-Alignment program in the GCG software package, using a gap weight of 5.0 and a length weight of 0.3.

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20. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide which is at least 80% percent identical to the amino acid sequence of SEQ ID NO:8 or 9, wherein said percent identity is calculated using the GAP program in the GCG software package, using a gap weight of 3.0 and a length weight of 0.1.

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21. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide which is at least 70% percent identical to the amino acid sequence of SEQ ID NO:10, wherein said percent identity is calculated using the GAP program in the GCG software package, using a gap weight of 3.0 and a length weight of 0.1.

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22. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide which is at least 70% percent identical to the amino acid sequence of SEQ ID NO:11, wherein said percent identity is calculated using the GAP program in the GCG software package, using a gap weight of 3.0 and a length weight of 0.1.

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23. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide which is at least 70% percent identical to the amino acid sequence of SEQ ID NO:12, wherein said percent identity is calculated using the GAP program in the GCG software package, using a gap weight of 3.0 and a length weight of 0.1.

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24. The nucleic acid molecule of claim 1 or 2, further comprising a vector or promoter effective to initiate transcription in a host cell.

20 25. The nucleic acid molecule of claim 24, wherein said promoter comprises an inducible promoter.

25 26. A nucleic acid probe for the detection, isolation, purification, enrichment, or amplification of a nucleic acid molecule encoding human OAT in a sample, wherein said nucleic acid probes are selected from the group of nucleic acid sequences set forth in, SEQ ID NO:2 from nucleotide 1370- 1638, SEQ ID NO: 3 from nucleotide 1370-1614, SEQ ID NO:4: from nucleotide 1-1107, SEQ ID NO: 5 from nucleotide 995-1662 and SEQ ID NO:6 from nucleotide 993-1623.

30 27. A nucleic acid probe for the detection, isolation, purification, enrichment, or amplification of a nucleic acid molecule encoding human OAT in a sample, wherein said nucleic acid probes are selected from the group of nucleic acid sequences encoding the polypeptide fragment selected from the group consisting of amino acids 132-136 of SEQ ID NO:8, amino

acids 132-136 of SEQ ID NO:9, amino acids 112-116 of SEQ ID NO:10, amino acids 136-140 of SEQ ID NO:11 and amino acids 135-139 of SEQ ID NO:12.

28. A recombinant cell comprising a nucleic acid molecule encoding a human OAT polypeptide wherein said nucleic acid molecule is selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6.

29. The cell of claim 28, wherein said cell is stably transformed.

10 30. The cell of claim 28 or 29, wherein said cell is a mammalian cell.

31. The cell of claim 28 or 29, wherein said polypeptide is a fragment of the polypeptide encoded by the amino acid sequence encoded by the nucleic acid sequence set forth in SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, or the amino acid sequence set forth in SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, or SEQ ID NO:12.

15 32. The cell of claim 28 or 29, wherein said nucleic acid is expressed from an inducible promoter.

20 33. The cell of claim 32, wherein said promoter is inducible with ecdysone.

34. An isolated, enriched, or purified human OAT polypeptide encoded by the nucleic acid sequence set forth in SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:6, or the amino acid sequence set forth in SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, or SEQ ID NO:12.

25 35. The polypeptide of claim 34, wherein said polypeptide is a fragment of the polypeptide encoded by the nucleic acid sequence set forth in SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:6, or the amino acid sequence set forth in SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, or SEQ ID NO:12.

36. The polypeptide of claim 34, wherein said polypeptide is isolated, purified, or enriched from a cell that comprises an endogenous nucleic acid molecule that encodes said polypeptide.

37. The polypeptide of claim 34, wherein said polypeptide is isolated, purified, or enriched from a cell that is transformed with a nucleic acid molecule that encodes said polypeptide.

38. The polypeptide of claim 34, wherein said polypeptide is chemically synthesized.

10 39. A labeled or unlabeled antibody or antibody fragment having specific-binding affinity to a human OAT polypeptide encoded by the nucleic acid sequence set forth in SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:6, or the amino acid sequence set forth in SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, or SEQ ID NO:12.

15 40. A hybridoma which produces an antibody having specific binding affinity to a human OAT polypeptide encoded by the nucleic acid sequence set forth in SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:6, or the amino acid sequence set forth in SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, or SEQ ID NO:12.

20 41. A method for identifying modulators of human OAT2A, human OAT2B, human OAT3, human OAT4, or human OAT5 polypeptide, said method comprising:

- (a) contacting said hOAT polypeptide with a test substance;
- (b) adding a substrate,
- (c) measuring the activity of said hOAT polypeptide; and

25 (d) if said substance decreases transport, determining whether said test substance is a modulator or competitive inhibitor of said hOAT polypeptide.

42. A method for identifying a modulator of human OAT2A, human OAT2B, human OAT3, human OAT4, or human OAT5 polypeptide in a cell, said method comprising:

30 (e) expressing an hOAT polypeptide in a cell;

- (f) contacting said cell with a test substance;
- (g) adding a substrate;

(h) measuring the activity of said hOAT polypeptide; and
(i) if said substance decreases transport, determining whether said test substance is a modulator or competitive inhibitor of said hOAT.

5 43. A method to screen for substrates or inhibitors of human OAT2A, human OAT2B, human OAT3, human OAT4, and human OAT5 using a cell stably transformed with an hOAT nucleic acid molecule and a competition assay, said method comprising:

(j) adding a test substrate to a cell line expressing said human OAT polypeptides;
(k) adding a substrate known to be transported by said human OAT polypeptides

10 in said cell line;

(l) measuring the ability of said test substrate to compete with the uptake of said substrate known to be transported by human OAT1, human OAT2A, human OAT2B, human OAT3, human OAT4, and human OAT5; and

(m) confirming whether said test substrate is an inhibitor or substrate.

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44. The method of claim 43, wherein said test substrate and/or known substrate are fluorescent or conjugated with a fluorescent labeled.

20 45. The method of claim 44, wherein said assay is evaluated using high-throughput screening.

46. A method for identifying substrates of human OAT polypeptides, said method comprising:

25 (n) loading a cell line expressing an hOAT polypeptide with a substance known to be effluxed from the interior of said cell as part of the antiporter activity of said hOAT polypeptide
(o) adding a test substrate to said cell line;
(p) measuring the efflux of said antiporter substance; and
(q) determining if said test substrate affected the efflux of said antiporter
30 substance.

47. The cell of claim 28 or 29, wherein said cell is a yeast cell.

48. The cell of claim 28 or 29, wherein said cell is an insect cell.

5 49. A method of preparing an hOAT polypeptide comprising:

(r) culturing the recombinant cell of claim 29 under conditions that permit expression of the hOAT polypeptide; and
(s) isolating said polypeptide.

10 50. An amphibian oocyte containing a nucleic acid molecule encoding for a human OAT polypeptide according to claim 2.

51. The amphibian oocyte of claim 50 that is a *Xenopus laevis* oocyte.

15 52. The nucleic acid molecules of claim 1 or 2, wherein said nucleic acid molecules comprise one or more regions that encode an hOAT polypeptide or an hOAT polypeptide fragment, where the hOAT polypeptide or the hOAT polypeptide fragment is fused to a non-hOAT polypeptide or epitope tag.

20 53. The nucleic acid molecule of claim 52, wherein said non-hOAT polypeptide or epitope tag is selected from the group consisting of glutathione-S-transferase, green-fluorescent protein and an amino terminal tag composed of histidine residues.

25 54. A method to identify toxic compounds transported by hOAT polypeptides comprising:

(t) expressing an hOAT polypeptide in cells;
(u) adding a test substrate to said cells; and
(v) determining if said cells are viable.

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